Evidence of an Increased Susceptibility to Lipid Peroxidation in Red Blood Cells of Chronic Renal Failure Patients

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Dear Sir,

The study of the red blood cells (RBC) oxidative metabolism in chronic renal failure (CRF), has recently become of interest, and until now, the results have not been very concordant. It has been shown [1], that there is an alteration in RBC pentose-phosphate shunt of patients with CRF undergoing hemodialysis. This would mean an alteration in the detoxification of the hydroxyl and peroxide radicals, with the ensuing peroxidation of the polyunsaturated fatty acids (PUFA) in the RBC membranes [2]. Consequently, an increase in the rigidity and deformability of these membranes is produced and, as a result, an increase in the susceptibility to hemolysis appears. The malonyl-dialdehyde acid (MDA), a short-chain aldehyde, is an intermediate product of the oxidation of PUFA, and has been reported as a good indirect method to measure the oxidative degradation of PUFA [3,4].

In order to investigate the susceptibility to the oxidative damage in the RBC, we determined the RBC levels of MDA in a group of patients affected by CRF. The study was performed on 58 subjects with CRF, divided into two groups. Group I consisted of 30 patients, 16 males and 14 females, aged 39–82 years (mean 62). The creatinine clearance was lower than 15 ml/min, (preterminal renal failure). All of them followed a low-protein and low-salt diet, adapted to tension levels. Group II consisted of 28 patients, 24 males and 4 females, aged 22–74 years (mean 51). All these patients were subjected to a regular hemodialysis program with a mean treatment duration of 37.3 months (range 27–150). The patients were dialyzed three times weekly, each session lasting 4 h. The dialyses were all done with a 0.9- to 1.3-m² hollow-fiber dialyzer and a standard dialysate with an acetate concentration of 38 mEq/l, and a dialysate flow rate of 500 ml/min. Water

was purified by an inversed-osmosis treatment. All patients were on a free diet, and none of them were taking any drugs that could interfere with the parameters considered, nor had they received any blood transfusion during the 3 months preceding the study. Patients presenting hepatic

disease, diabetes, systemic disease or neoplasias were excluded from the study. A third group (group III) was also considered. It consisted of 30 healthy adult controls, 18 males and 12 females, aged 18–55 years (mean 41). None of the 88 subjects considered were heavy smokers, their maximum being 5 cigarettes/day. RBC-MDA was determined by Stock and Dormandy's [4] method. All data in different groups were analyzed using the analysis of variance, Student's t test for paired data and linear regression analysis.

The mean MDA level in group III was 381.78 ± 65.93 nmol/g Hb. The levels were significantly higher ($p < 0.001$) in groups I and II (478.17 ± 79.6 nmol/g Hb and 510.18 ± 65.93 nmol/g Hb, respectively). No statistical differences were found when we compared the MDA values between groups I and II. The RBC-MDA levels were determined in patients of group I before and just after hemodialysis. A highly significant increase ($p < 0.001$) was seen at the end of the hemodialysis. In multiple linear regression between RBC-MDA levels, in patients of groups I and II, and the levels of hemoglobin, urea nitrogen, uric acid, creatinine, sodium, potassium, total calcium, phosphorus and alkaline phosphatase, no significant correlations were found except for uric acid, sodium and alkaline phosphatase ($p < 0.05$).

Our results show a very similar and significant increase in the MDA levels of patients with CRF and in patients undergoing chronic hemodialysis. It is therefore evident that RBC of patients with CRF have the same grade of susceptibility to lipid peroxidation, whether they are dialyzed or not. Unlike other authors [2], we

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found a significant increase when we compared the MDA values before and just after the hemodialysis session, having used the same dialysis scheme and material as the other authors, the only exception being in the means of obtaining the deionized water, which does not appear to be through inverse osmosis. The MDA increase after dialysis would be justified because of the oxidative stress to which the RBC are subjected and the subsequent increase in hemolysis during dialysis. This can be demonstrated because of the increase in plasma hemoglobin in the work of Lubrano et al. [5], hemoglobin which is corrected when they treat the patients with vitamin E, a well-known antioxidant substance. When we looked for a correlation between the MDA increase and different parameters which are usually altered in CRF, we only found a significant correlation between the plasma values of uric acid, sodium and alkaline phosphatase, which is difficult to interpret. Our results confirm the findings of other authors about the basal alteration of the RBC-oxidative defense system in patients with CRF and differ in the influence of the hemodialysis, because we found higher levels of MDA just after hemodialysis, probably because the RBC are subjected to a higher oxidative stress.

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